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Noninvasive MR-Guided HIFU Therapy of TSC-Associated Renal Angiomyolipomas

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14. ABSTRACT
This report is a summary of our three year's work on the proposed research. During this period, our effort was focused on technological development for thermal ablation in animals. We have established an MR-guided HIFU experimental system that enables simultaneous HIFU ablation and MR guidance in a physiological environment. However, it was found in our in vivo experiments that the established system is more suitable for large-animal models. As a result, mouse tumor ablation cannot be implemented in our studies. Based on this investigation, we are reformatting our research and planning for another effort to investigate MR-guided HIFU therapy of TSC-related renal angiomyolipomas in large animal models.

15. SUBJECT TERMS
MR-guided HIFU, renal angiomyolipoma, tumor, ablation, thermal therapy, TSC

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Introduction

At the Cincinnati Children's Hospital Medical Center (CCHMC), we are developing a non-invasive technique for human cancer therapy. This technique uses High-Intensity Focused Ultrasound (HIFU) to ablate tumors, and Magnetic Resonance (MR) guidance to monitor ablation. MR-guided HIFU enables “surgical procedures” to be performed deep within the body without incisions or punctures, providing a risk-free therapeutic approach to the management of cancers. The proposed research was an investigation on whether MR-guided HIFU can be used to improve the clinical management of TSC-associated renal angiomyolipomas.

TSC is a genetic tumor predisposition syndrome characterized by the growth of lesions in multiple organ systems. Approximately 80% of TSC patients develop renal angiomyolipomas, a type of lesion composed of variable amounts of fat, smooth muscle, and vascular tissue. Renal angiomyolipomas are often benign and present with multiple lesions in each kidney. Patients with renal angiomyolipomas may experience discomfort, flank pain, hydronephrosis, hematuria, and hypertension. These lesions can also lead to acute hemorrhaging or chronic loss of renal function. There exist clear needs for the development of a non-invasive therapeutic approach to the clinical management of this type of cancers.

The physical mechanisms underlying HIFU is that a HIFU transducer constructed with a concave shape and/or multiple elements has the ability to focus acoustic energy into a target volume having a diameter of a few millimeters. The focused acoustic energy induces a rapid rise in temperature (e.g. 70°C to 100°C), resulting in thermal necrosis of tissues in the target volume. Although HIFU offers the capability of thermal ablation, non-invasive thermal therapy is possible only if the focal spot of HIFU can be controlled within the body using the feedback information provided by medical imaging guidance. MR is superior to other imaging modalities because it provides both excellent soft-tissue visualization and the ability to monitor thermal delivery (temperature mapping). MR-guided HIFU first found applications in the clinical management of uterine fibroids. Up to date, over 7000 patients with symptomatic fibroids have been treated in the United States. This success demonstrated the potential capability of MR-guided HIFU in the clinical management of human cancers. However, subsequent research on the treatment of other types of human tumors met a fundamental challenge: Physiological complication (tissue inhomogeneity and dynamics) deep in the human body may reduce the efficiency of HIFU thermal delivery.

The proposed project was planned to experimentally investigate the ability of MR-guided HIFU to ablate renal angiomyolipomas in a mouse tumor model. Our first year's work led to the development of a small animal HIFU system with feedback control. In several in-vitro studies without motion concerns, we have demonstrated that the developed HIFU system offers the ability to focus acoustic energy within a small spot in a diameter of a few millimeters. During the second year, we proceeded with *in-vivo* studies and found that respiratory motion may be destructive to HIFU thermal treatment in the mouse kidneys. Although parallel imaging has been proposed and used to address this issue in this work, it was found that the performance of parallel imaging is not sufficient for this application because coil array configuration is limited by small mouse anatomy. In our third year's effort, the research plan was accordingly changed because of the finding of limitation in small animal model. We acquired a new clinical 256-channel HIFU system for human thermal therapy and a new Ingenia 1.5 Tesla MRI scanner from Philips HealthCare. Using the new instrumentation, we established a large animal MR-guided HIFU system. It was demonstrated that this new system offers the ability to ablate small lesions in an environment with physiological complication in a large animal model.

This report is a summary of our three year's work on the proposed research. The summary will focus on the technical challenges we met and provide details about why this challenge cannot be overcome using the proposed techniques. In addition, we provide a research plan to continue this research in our institution after the completion of the proposed DOC grant work.

Body

Over the last three years, our effort was focused on the technological development for MR-guided HIFU therapy in an animal model (Tasks 1 and 3 in the proposal). Due to the finding of the anatomy limitation in mice MRI coil development, mouse cancer model was not used eventually. In the third year, we developed a large animal MR-guided HIFU system. Using this system, we demonstrated that the thermal ablation of a small lesion in a pig is feasible. In the coming time (after the completion of this DOD grant), we are planning to develop a large animal TSC-related renal angiomyolipoma model for preclinical experiments.

Proposed Task 1: Design and development of an MR-guided HIFU experimental system for thermal ablation in a phantom study.

1a. Hardware development.

A coil array will be designed and developed for abdominal imaging in mice. The number of receive channels will be determined experimentally for optimum SNR and imaging acceleration performance in mouse imaging. This coil will be integrated with a HIFU system for small animal research in a Philips 3.0 Tesla multi-channel MR imaging system.

1b. Software development.

Dynamic parallel imaging and motion correction methods will be developed on Philips 3.0 Tesla multi-channel MR imaging system. Real-time reconstruction will be implemented. Four major imaging methods, T_1 weighted imaging, T_2 weighted imaging, stiffness weighted imaging, and phase imaging, will be developed using parallel imaging. Data processing methods will be developed to extract multi-source information, including lesion position, temperature, acoustic force under HIFU, and tissue destruction in therapy, from real-time MR images. A control algorithm will be developed to dynamically optimize the localization and power of HIFU focal spot based on real-time and multi-source feedback information.

1c: Test of basic function.

MR-guided HIFU experimental system will be tested and optimized in a phantom study. Its ability to ablate a pre-selected target in the phantom will be evaluated.

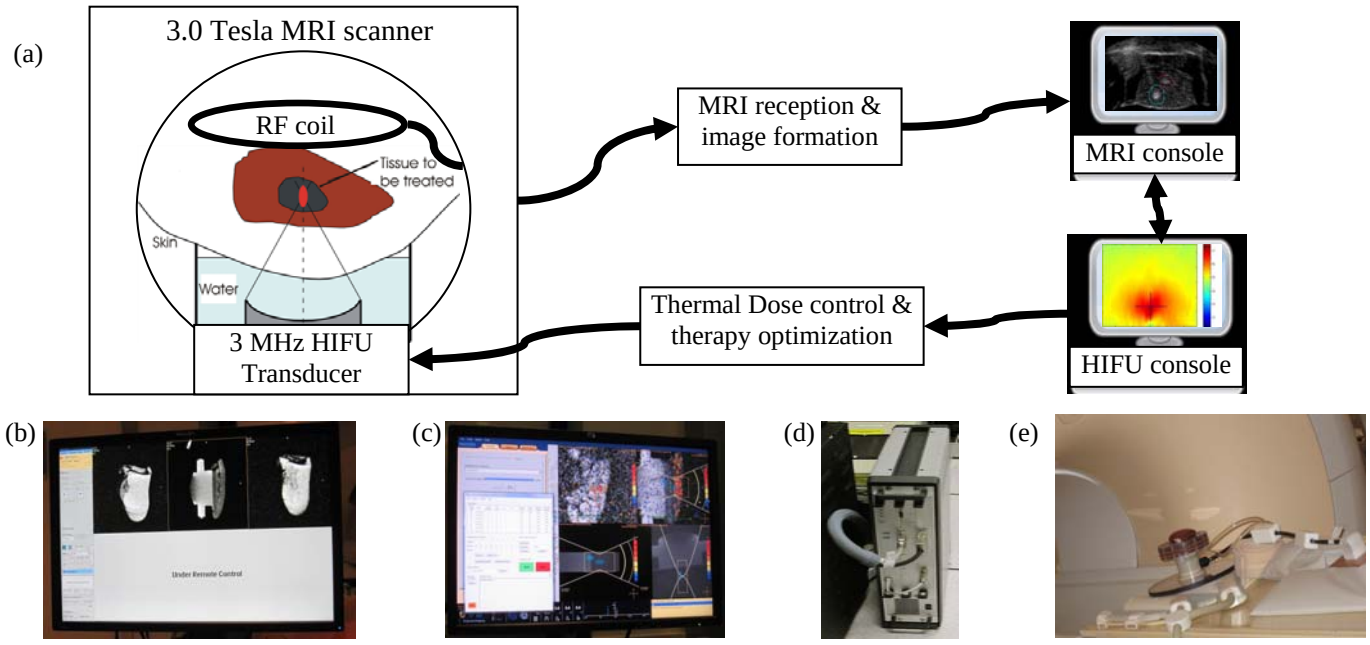
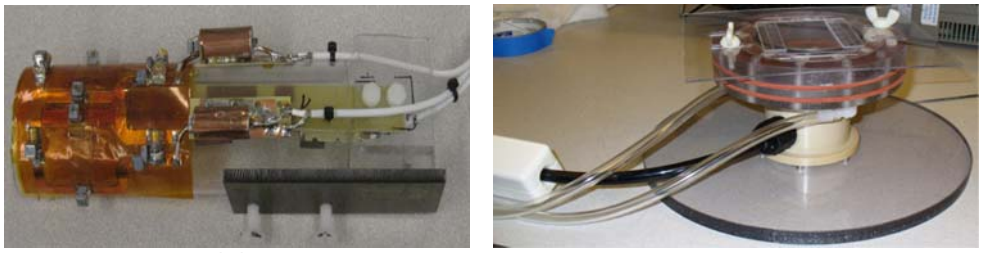


Figure 1. *A feedback control system for preclinical thermal therapy was established using MR-guided HIFU in the CCHMC IRC. The feedback control loop is formed using a 3.0 Tesla 32-channel Philips Achieva MR scanner (Philips HealthCare, Best, the Netherlands) and a Philips small-animal HIFU system (Philips HealthCare, Vantaa, Finland). This system uses an eight-channel 3 MHz sectored transducer (IMASONIC, Voray sur l'Ognon, France) for acoustic transmission. (a) Experimental setup scheme. (b) MRI console. (c) HIFU console). (d) High-efficiency generator for HIFU transducer. (e) Transducer, cables and phantoms inside the MRI scanner.*

Research accomplishment: A small-animal HIFU system (Philips HealthCare, Vantaa, Finland) was purchased and installed on the IRC Philips 3.0 Tesla MRI scanner at the Cincinnati Children's Hospital Medical Center (Figure 1). This system includes an eight-channel 3.0 MHz sectored ultrasound transducer, a high-efficiency generator for acoustic power control, and a stand-alone console that can be used to control the HIFU power transmission and communicate with the MRI scanner. Figure 1 shows the experimental setup scheme and pictures for thermal ablation in phantoms and animals. This setup allows the HIFU console to synchronize MRI scanning when running HIFU thermal ablation. The acoustic power delivery from the HIFU transducer can be dynamically updated by the HIFU console based on MRI information. This provides a feedback control for the thermal delivery deep within the body.

A small-animal MRI coil was constructed (Figure 2a). This coil provided better SNR for mouse imaging than other coils on the IRC Philips 3T MRI scanner. The SNR gain factor was estimated to be ~ 3 over the commercial small-animal coil provided by Philips HealthCare. A mechanic stage (Figure 4b) was built for holding/stabilizing the animal/phantom and the coil in HIFU experiments within the MRI scanner. This stage has an empty space inside and is sealed outside. The sealed space is used to accommodate water for interfacing acoustic pathway between the transducer and the target. There are two tubes (Figure 4b) connected to the internal space inside the stage. These tubes are used to fill the water into the stage and remove the air bubbles in the water.



(a) (b)

Figure 2*. An MRI coil (a) was built for mouse imaging on Philips 3T scanner. A mechanic stage (b) was constructed for holding/stabilizing the mouse and the coil within the MRI scanner. Inside the stage, water will be used as the interface between the HIFU transducer and the animal.*

All the hardware was tested on the MRI scanner. The test demonstrated that the hardware is MR compatible. In addition, we experimentally compared our MR imaging results with those using commercial hardware. The experiments showed that our hardware offers better MR imaging quality than commercial hardware provided by Philips HealthCare. The new hardware we developed was integrated with MR scanner system.

The software development work was accomplished in collaboration with Philips HealthCare during the last several months. This collaboration includes the setting up of the imaging protocols for animal HIFU ablation, the configuration of software for feedback control of HIFU transducer, and the verification of MR guidance for HIFU ablation. Currently, we have a software package installed on the HIFU console. This package includes a standard Philips clinical software, Sonalleve (*Philips HealthCare, Vantaa, Finland*), and a small-animal HIFU software. The prior one provides the capability of communication with MRI console and processing MRI data. The latter one provides the capability of communicating with the HIFU generator and extracting information from Sonalleve. This package provides a feedback control algorithm for HIFU ablation. A standard Philips MRI protocol was installed on Philips 3T MRI scanner. These protocols provide the capability of imaging animals with different strategies during HIFU ablation and monitoring the thermal delivery in real time. An echo-planar imaging protocol was developed in combination with our new MR coil and used in MR guidance for HIFU ablation. The temporal resolution for this sequence is ≤1 second.

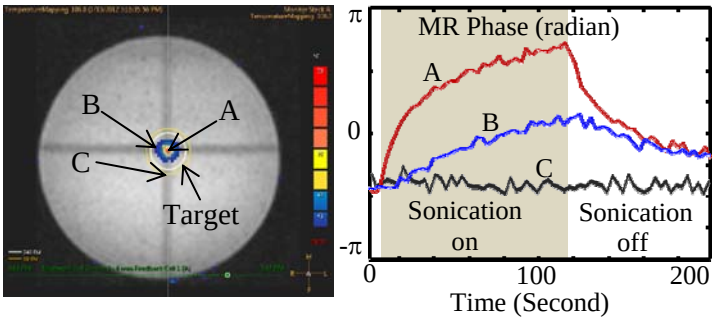


Figure 4. *HIFU thermal ablation and temperature mapping in a homogeneous phantom. A HIFU lesion of ~ 2 mm can be formed using feedback control in Figure 1. The plots show MR phase signals change with temperature and provide an approach to tracking and optimizing HIFU thermal delivery. The color maps overlaid on the MR image gives the temperature mapping in HIFU ablation.*

The developed hardware and software were tested in phantom experiments. As shown in Figure 4, a HIFU ablation experiment was conducted using a homogeneous gel phantom. A HIFU lesion of ~ 2 millimeter was successfully developed within the target region. The MR phase signals showed dynamic variation associated with temperature rise within the HIFU lesion, indicating the temperature can be effectively monitored during the ablation. The small-animal MR-guided HIFU experimental system was also tested in in-vitro studies. Figure 5 shows an experimental study on MR-guided HIFU using a piece of pig liver. It was found that HIFU offers the capability of deliver ultrasound energy into a small local spot of ~ 2 millimeters. This demonstrates the potential of HIFU to ablate tumors deep within the mouse body.

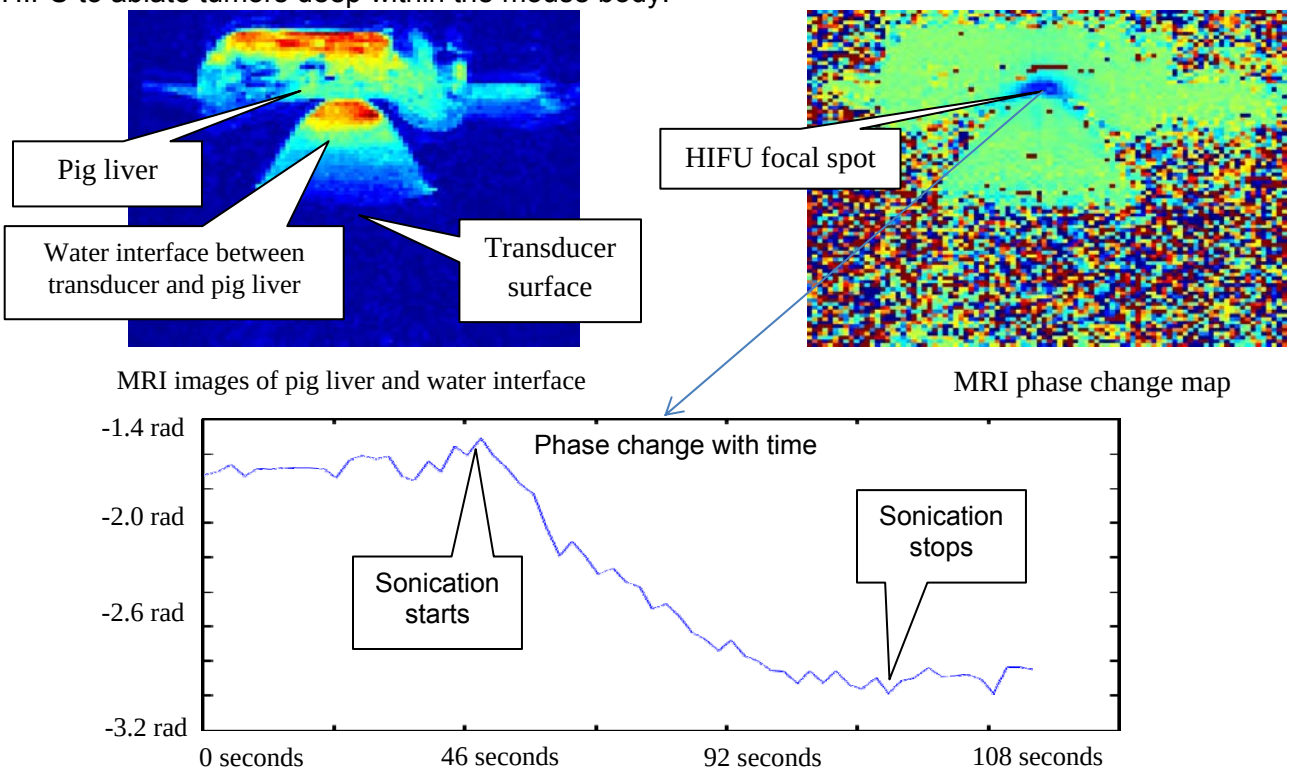


Figure 5. *An in-vitro study (ablation of pig liver) using the established MR-guided HIFU system in Figure 1. The MR phase change mapping shows the acoustic energy is focused within a small local spot of ~ 2 millimeters. The plot shows the phase change with sonication in the center of focal spot. This study demonstrates the basic function of the experimental system we developed in the first year.*

Proposed Task 3: Optimization of the MR-guided HIFU system.

The real-time MR guidance of renal targets will be optimized. The adaptive control system will be optimized for maximizing the effectiveness and safety of HIFU thermal ablation. 10 mice will be used. This *in-vivo* test is the preparation phase for the following systematic evaluation of MR-guided HIFU therapy in task 4.

3a. Optimization of real-time MR guidance.

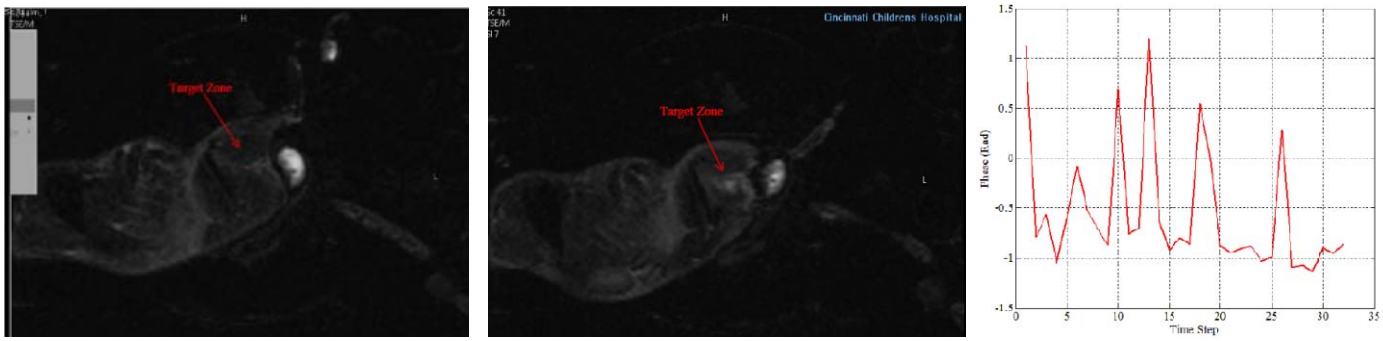
Parallel imaging will be optimized to improve imaging speed and minimize motion artifacts in free-breathing mice. Specifically, the optimization will be performed to improve four major imaging methods, T_1 weighted imaging, T_2 weighted imaging, stiffness weighted imaging, and phase imaging. It will be demonstrated that these imaging methods can provide accurate and real-time information about HIFU therapy delivery.

3b. Optimization of the adaptive control system for HIFU.

In free-breathing mice, the adaptive control system will be optimized to improve the localization and power of HIFU focal spot dynamically based on real-time MR guidance. It will be demonstrated that HIFU lesions can be effectively created irrespective of respiratory motion. The safety limit for thermal dose in HIFU ablation will also be determined. This safety limit will be used to determine the thermal dose for MR-guided HIFU therapy in the following task 4.

Research accomplishment: Following our work in the first year, we conducted a series of in vivo experiments. Experimentally, we found that the proposed parallel imaging technique cannot provide good performance due to coil array limitation. Figure 6 shows a HIFU ablation result using the experimental system

and a healthy animal. It was found that HIFU energy was successfully delivered into the animal body while temperature information was not able to be collected in real time using parallel imaging techniques. Our further investigation shows that the coil array we developed cannot provide good parallel imaging performance because the coil elements have to be larger than the mouse anatomy and positioned in a certain distance to the mouse. This configuration was practically limited by two factors: First, acoustic power transmission requires an open space to the abdominal region of the mouse. Since water has to be used to provide acoustic interface between the transducer and the mouse body, coil elements cannot be positioned close to the imaging target zone. Second, the coil elements have to large enough to achieve certain RF penetration due to the positioning limitation. As a result, spatial variation of multi-channel coil sensitivity was low, which significantly reduces the spatial encoding of coil sensitivity within the mouse body. Without sufficient imaging speed, dynamic imaging provides low image quality and temperature information (phase change of MR images) was distorted by imaging artifacts.



T1 image before ablation | T1 image after ablation | Temperature mapping

Figure 6. *Mouse HIFU ablation. Using the experimental system in Figure 1, HIFU ablation was performed in a healthy mouse. T1-weighted MR images were collected to determine whether a HIFU lesion was formed in the target zone. By comparing T1-weighted images before and after ablation, the contrast difference was found, implying HIFU lesion was produced deep inside the animal body. However, dynamic MR images were not able to provide accurate temperature information for real-time feedback control.*

Project redirecting: Because of the finding of the anatomy size limitation in mouse MRI, we launched two efforts to redirect the project. The first effort was to develop a new type of coil arrays for improved mouse MRI by collaborating with Dr. Qiming Zhang's group in Pennsylvania State University. However, satisfactory results were not generated till the end of this project in this effort (See appendix 1).

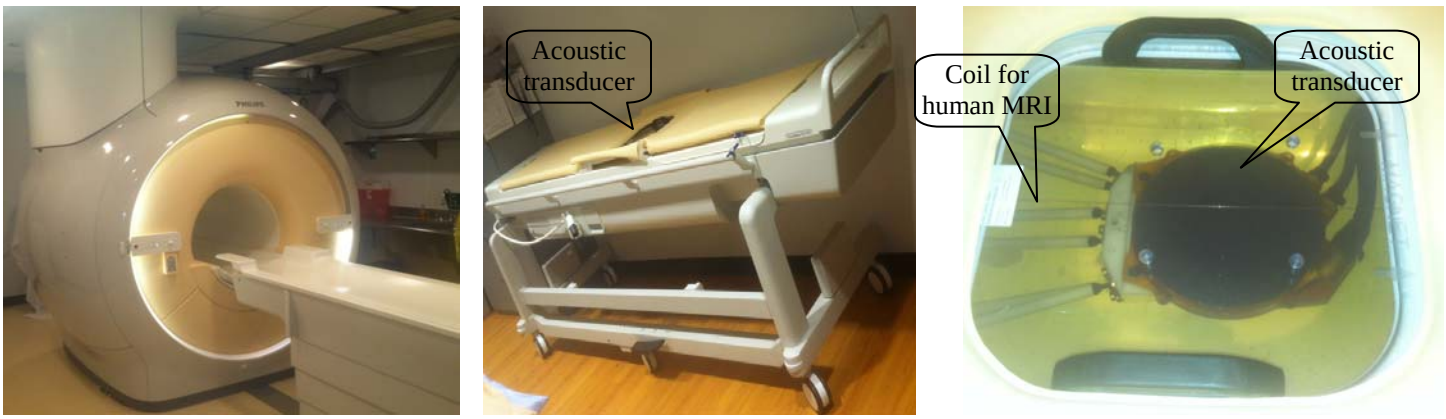


Figure 7. *Human HIFU and 1.5 Tesla Human MRI: The human HIFU has a 256 element acoustic array transducer (right figure). This transducer is embedded in a patient table (middle figure). The table can be placed in the 1.5 Tesla Human MRI scanner. A large animal can be placed on the patient table and HIFU experiments can be implemented. HIFU system can communicate with the MRI scanner console using commercial software provided by Philips HealthCare.*

Our second effort was to use a large animal model in the investigation of MR-guided HIFU performance. This effort was made possible owning to the support provided by CCHMC. In the third year of this project, CCHMC

imaging research center made a significant contribution to our research in MR-guided HIFU. A 1.5 Tesla Ingenia MR imaging system with human HIFU system was purchased from Philips HealthCare and installed in the imaging research center (Figure 7). This human HIFU system has 256 acoustic elements and offers the capability of moving the transducers in an arbitrary direction. More importantly, the commercial HIFU system allows the use of digital coil arrays provided by Ingenia system. As a result, this new system provides much better performance than the small animal HIFU system.

Figure 8 shows our experimental results using the human HIFU/MRI scanner with a pig model. In this experiment, we successfully focused the acoustic energy into a small spot of ~3mm deep in the pig body (red colored spot). More importantly, temperature information was collected in real-time using parallel imaging MRI techniques (right figure in Figure 3). It was demonstrated that MR-guided HIFU can introduce a rise of temperature of ~35 degree deep in a large animal model.

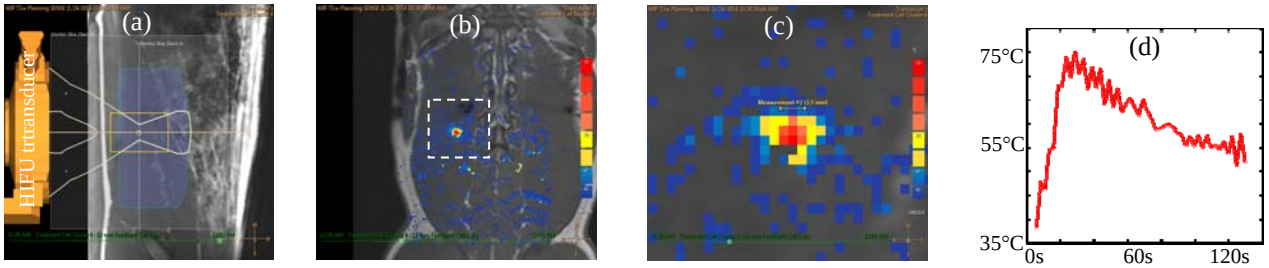


Figure 8. *Pig HIFU ablation. (a). Experimental setup. The center of the cross in the sagittal image indicates the spot which HIFU treatment is targeted at. (b). The MR image indicates the lesion HIFU generated (red-color region). (c). Zoomed image in the dashed-line rectangular box of (b). The measurement shows that the HIFU lesion is ~ 3.5 mm. (d). The time plots of temperature mapping at the HIFU lesion center demonstrate MR gives an adequate feedback.*

Because of the limitation of time and budget provided by this DOD grant, we cannot complete all the tasks. However, we have recognized the issues that cannot be understood without the experiments conducted in the last 3 years. We are planning to use a large animal model to continue the proposed research in this DOD proposal.

Key Research Accomplishments

1. A small animal MR-guided HIFU experimental system was established at the Cincinnati Children's Hospital Medical Center (CCHMC) Imaging Research Center (IRC).
2. Thermal ablation and MR guidance capability was demonstrated using the established experimental system in in-vitro studies.
3. MR imaging speed using EPI sequence was found sufficient for real-time feedback in HIFU thermal delivery. This addressed the challenge arising from that respiratory movement in mice.
4. We found that the water interface between the transducer surface and the animal body is crucial to the thermal delivery. To address this issue, we constructed a mechanic stage that can provide a water interface for ultrasound wave propagation.
5. All the hardware and software are ready for mouse ablation experiment. We will make a final adjustment of the system in the coming two months before the start of mouse ablation.
6. The small-animal MR-guided HIFU experimental system was demonstrated functional in in-vitro studies. We will proceed our animal studies in the second year.
7. We found a technical challenge that arises from the coil array limitation posed by small animal anatomy and acoustic power transmission.
8. A large animal MR-guided HIFU experimental system was established using a human HIFU and 1.5 tesla MRI scanner. We are planning to transfer the animal experiments to this system.

9. A mathematical model was developed to investigate adaptive control algorithms in mouse HIFU ablation (see the annual report in 2013).

Reportable Outcomes

1. We have collaboratively developed a mathematical model with Dr. Donald French's group in the Mathematical Department at the University of Cincinnati (Appendix 1). This model provides a tool to investigate adaptive control problems in mouse HIFU treatment.
2. We have developed our collaboration Dr. Qiming Zhang's group. We are collaboratively developing a new type of magnetoelectric sensors that may be used to replace coil array in our current HIFU system for mouse ablation.
3. Based on our preliminary results we obtained in this study, we applied for St. Baldrick foundation research grant. This grant was awarded in July 2012 and provided a support on the purchase of a needle hydrophone system that can measure the acoustic pressure in in-vitro studies. This will provide a direct way to evaluate HIFU transmission in soft tissue and a new technique to monitor HIFU ablation in real time. We are working on how to integrate the new project with the DOD project in order to deliver the best experimental outcomes in a more efficient way.
4. Based on this study, we have developed our collaboration relationship with two research groups at the University of Cincinnati: Dr. Donald French's group [1-2] and Dr. Christy Holland's group [3]. Dr. French is working on inverse imaging problem for HIFU treatment planning and Dr. Holland is working on cavitation mechanisms in cardiac applications of HIFU. We are working on combining these different research projects together for enhancing our ongoing MR-guided HIFU project.

Conclusion

In summary, we have found new challenges in this project. From our preliminary investigation using *in-vivo* studies, we understood the physical mechanisms underlying the technical challenge and found a solution to addressing this technical challenge. We expect to achieve our goals proposed in this proposal using a different experimental strategy in the coming time.

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Appendix 1

See the following pages.

Preliminary Results of Shear Mode Magnetoelectric Sensor

Qiming Zhang

Magnetoelectric effect is a material phenomenon featuring the interchange between magnetic and electric energies or signals. Ultra sensitive magnetic sensor operating at room temperature can be realized by the magnetoelectric coupling; During the past two months, ME sensor project was focused on: 1) shear mode ME sensor design; 2) holder design for Terfenol-D/PVDF structure; 3) measurements for Terfenol-D/PVDF shear mode ME sensor. A "double" shear mode Magnetoelectric (ME) sensor is designed and fabricated, the ME coefficient and frequency measurements are performed and the preliminary results will be demonstrated and discussed in this report.

Basic Principles of ME sensor

The principle of the ME sensor is that a magnetic field induces a strain in the ferromagnetic substance (NiFe2O4, Metglas, Terfenol-D, TbFe2, etc) by magnetostriction; and the strain is then coupled to the piezoelectric substance (Pb(Zr, Ti)O3, PMNPT, PVDF, etc), resulting in an electric output signal, as illustrated in Fig.1. The ME sensor has two working modes because of the nonlinearity of ferromagnetic substance's magnetization: linear region with DC bias and AC modulation without DC bias, a more detailed explanation could be found in Ref.1.

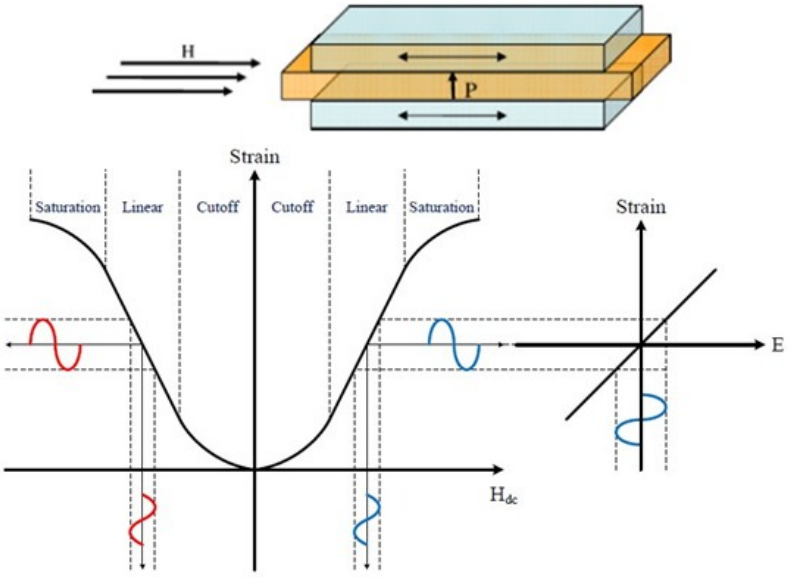

Fig.1 Schematic representation of the ME effect in the composites utilizing the product property

Shear Mode Sensor and Related Holder Design

Fig.2 is the schematic design of the "double" shear mode ME sensor, the polling of piezo layer (PVDF) is in the -x direction and the magnetization of the magnetoelastic layer (Terfenol-D) is in the same direction; a DC bias field is applied perpendicular with a 1.015 Oe AC magnetic signal; the AC signal will generate strain via a shear mode magnetostriction (d15 mode) as illustrated in Fig. 2, this shear strain will be coupled to the piezoelectric layer via piezoelectricity and generate charge at top and bottom surfaces; since the polling of PVDF is also in -x direction, from the piezocharge constant matrix as Eq.1, we can find that the PVDF is also working at shear mode. Tab.1 is the piezocharge/piezomagnetic constants of Terfonol-D/PVDF, we can find that the shear mode piezo-magnetic constant d15 is much larger than d33 and d31, while the piezo-charge constant is a little smaller than d33 but larger than d31; this is why the performance of our "double" shear mode ME sensor is better and we would like to apply this structure in our future ME sensor project.

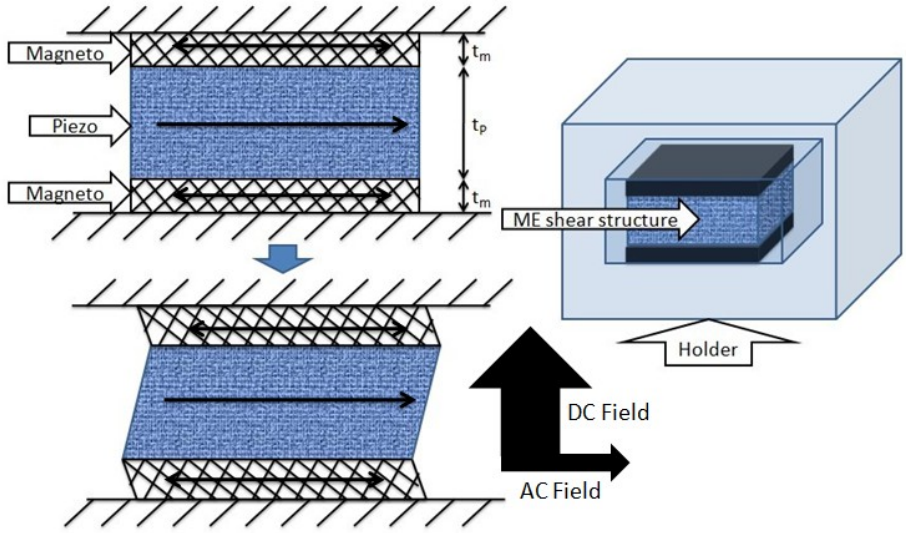

Fig.2: Schematic design of the "double" shear mode ME sensor

$$\begin{bmatrix} D_1 \\ D_2 \\ D_3 \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 & 0 & d_{15} & 0 \\ 0 & 0 & 0 & d_{15} & 0 & 0 \\ d_{31} & d_{31} & d_{33} & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} T_1 \\ T_2 \\ T_3 \\ T_4 \\ T_5 \\ T_6 \end{bmatrix} + \begin{bmatrix} \epsilon_{11} & 0 & 0 \\ 0 & \epsilon_{11} & 0 \\ 0 & 0 & \epsilon_{33} \end{bmatrix} \begin{bmatrix} E_1 \\ E_2 \\ E_3 \end{bmatrix}$$

Eq.1: Piezocharge constant matrix equation for PVDF

Piezo-magnetic constant (10^{-9} mA^{-1}) of Terfenol-D			*Piezo-charge constant (pC/N) of PVDF*		
d_{31}	d_{33}	d_{15}	d_{31}	d_{33}	d_{15}
-5.3	*11*	*28*	*21*	*-32.5*	*-27*

Tab.1 Piezocharge/piezomagnetic constants of Terfonol-D/PVDF

Fig.3 is a block diagram of ME sensor system, which has a picture of our holder design; the holder is made with alumina, it really takes us a while to find the right material for the holder: The material should have large stiffness while not conductive, we have tried copper, glass, nylon and some other materials and finally applied alumina for this design.

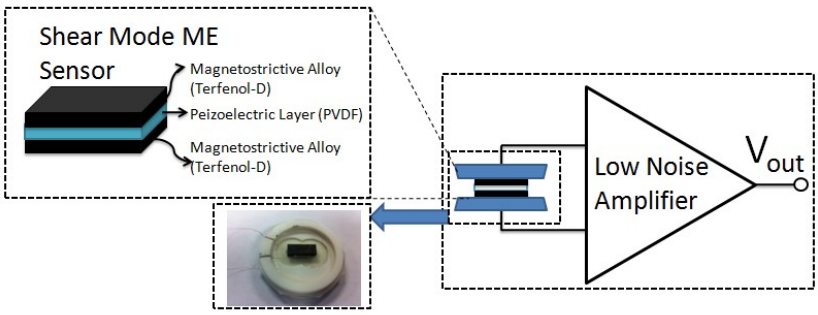

Fig. 3 Block diagram of ME sensor system

Results and Discussion

The following are the preliminary results we have from the shear mode ME sensor system; Fig.4 is the output and ME coefficient measurements and Fig. 5 is frequency scanning. During the ME coefficient measurement, we will increase the DC bias field from 0 to positive 2300Oe and then back to 0 (Fig. 4a); after that we will increase it to negative 2300Oe and back to 0 (Fig. 4b).We can find: 1) there will be an output even the DC bias is 0 which means the sensor has self bias (Fig.4c) compared with the current push-pull or TL/TT/LL mode ME sensors; 2) the shear mode sensor will have a larger saturation point than the current push-pull or TL/TT/LL mode ME sensors (Fig.4c). And also we did the calculation for ME coefficient (Fig.4d) and our sensor could reach 2953 mV/cm Oe (without saturation) compared with 480 mV/cm Oe of LT mode Terfenol-D/PVDF ME sensor reported by Dr. Wuttig's group (The University of Maryland) (Ref.2). This performance is excellent and much better than any reported Terfenol-D/PVDF ME sensor system.

Fig.5 is the frequency scanning measurements; Fig.5a is impedance scan and Fig5b is the output from ME sensor system when the working frequency is increased. We can find that the Output will increase with frequency which means the ME coefficient will be further improved when we increase the AC frequency: The output is 110.6mV @ 62.5KHz compared with 28.05@1KHz, it is already 3.94 times larger and will increase even more when the frequency is further increased. In another way, we can say that the shear mode has the potential to be used for high frequency measurements.

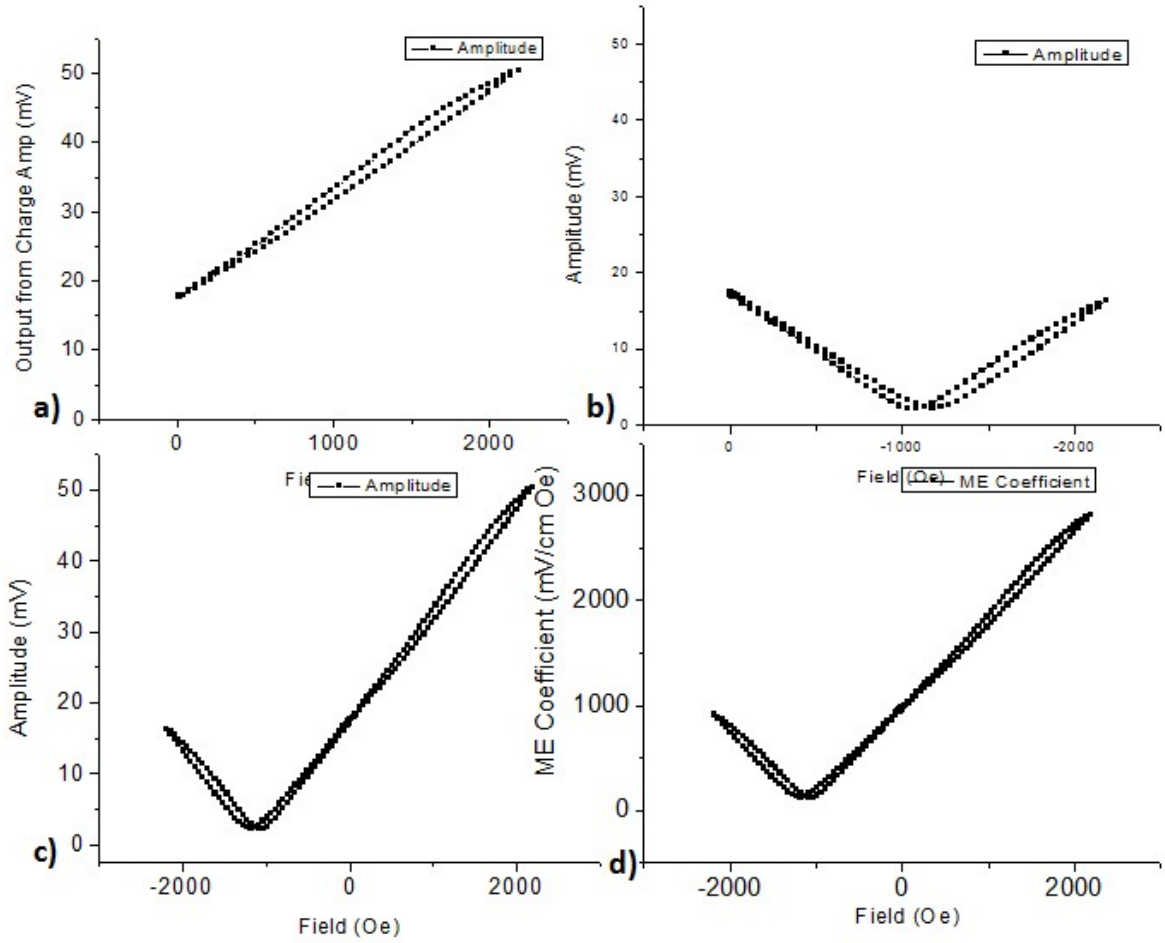

Fig. 4 Output and ME coefficient measurements

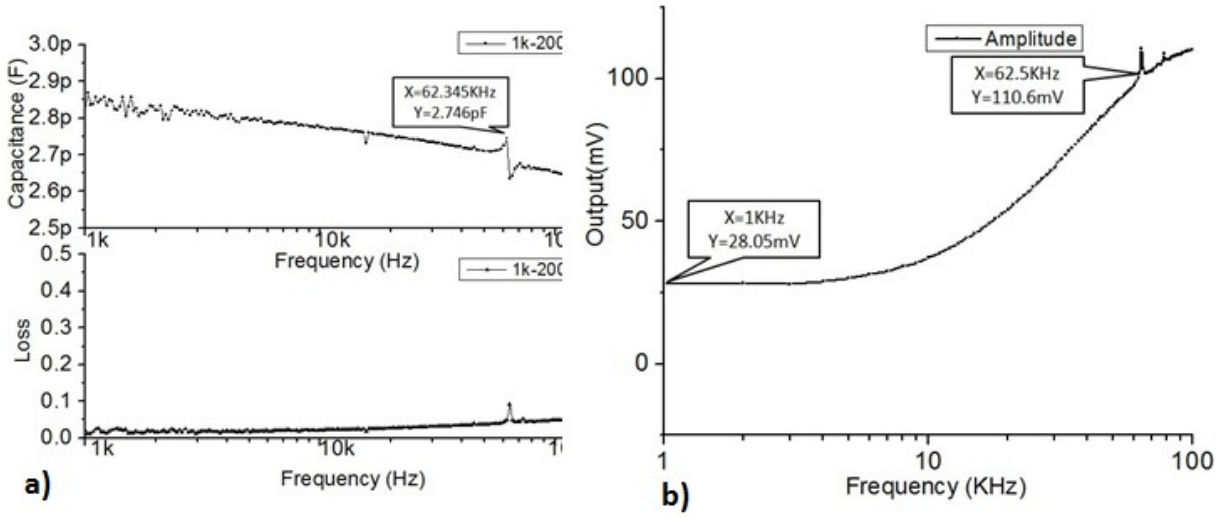

Fig. 5 Frequency scanning measurements

Conclusions and Future Work

From the preliminary results, we can find out that the shear mode ME sensor system have some advantages, such as 1) self bias; 2) large ME coefficient; 3) increased saturation field; 4) the performance will be better at higher frequency; in this case, the shear mode ME sensor is a good candidate for high frequency/tiny magnetic field measurements.

We plan to do the following in the next few months: 1) understanding the details of shear mode ME sensor (We should derive the equations to calculation the output and signal to noise ratio (SNR), etc); 2) we should build a mason circuit model or relevant circuit models for resonance ME sensor analysis. Meanwhile we will publish some papers based on our shear mode ME sensor measurements, no one has reported this yet, most of current "shear mode" only adopt "shear mode piezo effect", we are the first group trying to use the "double" shear mode for ME sensor system design.

References

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